

REMARKS

Claims 14-24, as amended, appear in this application for the Examiner's review and consideration. Claims 1-13 are canceled while claim 14 has been amended to recite that the composition is topically applied to pretreated skin without the application of electrical energy, and that the cartridge is removably attached to the main unit for applying the electrical energy and thereafter can be detached. Support for the former recitation is found in the specification, e.g., in paragraphs [0086] and [0087] as well as in the examples, while support for the latter recitation is found e.g., in paragraphs [0024] and [0066] and the drawings of the published application. Since no new matter is introduced by this change, the amendment should be entered at this time.

After receipt of the current office action, Applicant's docketing clerk contacted the Examiner to inquire as to why the claims submitted on March 10th were not considered even though the Office Action was not mailed until March 12th. The Examiner noted that she had completed her review of the previously submitted claims before March 10th and that her work had been "counted" so that she could not review the claims that were submitted before the mailing of the current Office Action. It is respectfully submitted that this is not a correct way to proceed such that, at a minimum, any further rejection of the current claims should not be made final since the Examiner did not review the claims that were clearly submitted prior to the mailing of the current Office Action. In any event it is believed that the claim amendments and distinctions over the cited art place all claims 14-24 in condition or allowance.

The cancellation of claims 1-13 thus renders moot all rejections of those claims.

Claims 14-17, 19, and 22-24 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over "Radiofrequency-driven skin microchanneling as a new way for electrically assisted transdermal delivery of hydrophilic drugs" to Sintov (referred herein as "Sintov") in view of U.S. Patent No. 6,302,874 to Zhang (referred herein as "Zhang"). The Office Action indicates that Sintov teaches a system and methods for transdermal delivery of hydrophilic drugs comprising: generating a plurality of microchannels in the skin of the subject using an apparatus comprising: an electrode cartridge comprising a plurality of electrodes to be oriented generally perpendicular to the skin; and a main unit which is adapted to apply radiofrequency energy between two or more electrodes, generating current flow to enable

ablation of the stratum corneum to produce microchannels that have a diameter of 10-100 microns and a depth of 20-300 microns, wherein the electrode cartridge is configured for removable attachment to the main unit and can be detached and discarded after use. The Office Action further indicates that Sintov teaches topically applying a water-soluble composition via a patch, but acknowledges that Sintov fails to teach a composition devoid of permeation enhancers. For this reason, Zhang is cited as a teaching of how to produce transient pores in the skin to facilitate the transdermal delivery of a cosmetic agent composition comprising a cosmetic agent, an acceptable carrier that is devoid of permeation enhancers. The Office Action further states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the device and method of Sintov to apply the patch containing the cosmetic agent and carrier as taught by Zhang to improve the appearance of the skin.

Applicants respectfully disagree with these statements. What Sintov actually discloses is a method for transdermal delivery of granisetron hydrochloride and diclofenac sodium through aqueous microchannels into the blood (see p. 312, right column of Sintov). Sintov further discloses that the micro-channels created by radio-frequency currents cross the stratum corneum deep into the epidermis (Abstract; p. 316 right column; and Fig. 1 of Sintov). Sintov neither discloses nor suggests a method for treating a skin condition comprising generating micro-channels in an area of the skin of a subject and topically applying a cosmetic or dermatological composition comprising at least one water-soluble, poorly water-soluble or water insoluble cosmetic agent. Neither granisetron hydrochloride nor diclofenac sodium is understood as being a cosmetic agent by a person of ordinary skill in the art. Furthermore, these compounds are delivered into the blood of the patient, and thus are not intended to have any effect on the condition of the subject's skin.

Zhang does not remedy the deficiencies of Sintov. Zhang discloses applying an electric pulse to a region of the skin substantially contemporaneously with a composition comprising L-ascorbic acid (see col. 3, lines 61-64 of Zhang). The electric pulse creates transient aqueous pathways in lipid bilayers and delivers an effective amount of L-ascorbic acid (col. 2, lines 65-67; and col. 5, lines 36-38 of Zhang). Thus, even if one combines Sintov and Zhang, he would obtain a method for transdermal delivery of L-ascorbic acid comprising generating micro-

channels and applying L-ascorbic acid for delivery into the subject's blood, wherein the delivery of L-ascorbic acid is achieved by electric pulse.

In contrast, the present invention discloses a method for treating a skin condition in a subject which comprises the steps of:

(i) pretreating skin by generating micro-channels in an area of the skin of a subject by an apparatus which comprises:

(a) an electrode cartridge comprising a plurality of electrodes to be oriented generally perpendicularly to the skin with electrode ends in the vicinity of the skin; and

(b) a main unit comprising a control unit which is adapted to apply electrical energy between two or more electrodes when the electrodes are in vicinity of the skin, typically generating current flow or one or more sparks, enabling ablation of the stratum corneum in the area beneath the electrodes, thereby generating in the stratum corneum micro-channels having a diameter of about 10 microns to about 100 microns and a depth of about 20 microns to about 300 microns; and

(ii) topically applying to the pretreated skin without the application of electrical energy a cosmetic or dermatological composition comprising at least one water-soluble, poorly water soluble or water-insoluble cosmetic agent and a cosmetically or dermatologically acceptable carrier to the area of the skin in which the micro-channels are present so as to improve the skin condition of the subject, the cosmetic or dermatological composition is devoid of permeation enhancers, with the electrode cartridge configured and dimensioned for removable attachment to the main unit and being removably attached to the main unit for applying the electrical energy and thereafter being detached.

It should be appreciated that generating hydrophilic micro-channels by the apparatus of the present invention (see paragraphs [0030] to [0033] and [0062] of the published application) was found to be unexpectedly effective for delivering water-soluble, poorly water-soluble and water-insoluble cosmetic agents for treating skin conditions (see paragraphs [0016], [0045], and [0062] of the published application). According to the present invention, the cosmetic agent is placed over the area where micro-channels are present after removal of the apparatus; no electrical pulse is applied to the cosmetic composition as the cosmetic agent is delivered efficiently by diffusion only (see paragraph [0026] and the examples of the published

application). Thus, claims 14-17, 19, and 22-24 are patentable over Sintov in view of Zhang, and the rejection of these claims under 35 U.S.C. 103 (a) should be withdrawn.

Claims 18, 20 and 21 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Sintov in view of Zhang as applied to claims 14, and 15, and further in view of U.S. Patent No. 6,447,410 to Henley (referred herein as "Henley '410"). The Office Action indicates that Sintov in view of Zhang teaches the device and method of claim 15 but fails to teach wherein the cosmetic agent is hydroquinone. The Office Action further indicates that Henley '410 teaches delivery of cosmetic agents to the skin that can include hydroquinone in order to remove pigmentation from hyperpigmented areas of the skin. The Office Action states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the device and method of Sintov in view of Zhang to deliver hydroquinone as taught by Henley '410. The Office Action further states that in reference to claims 20 and 21, Henley '410 teaches delivery of antibacterial agents to the skin in order to inhibit bacterial growth. The Office Action further states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the device and method of Sintov in view of Zhang to include an antibacterial agent in the composition as taught by Henley '410 in order to inhibit bacterial growth.

Again Applicants disagree with these statements. As indicated above, Zhang does not remedy the deficiencies of Sintov such that the combination of Zhang and Sintov does not result in the invention defined by independent claim 14. Henley '410 does not remedy the deficiencies of Sintov and Zhang. Henley '410 discloses a portable, self-contained, hand-held electrokinetic device for delivering or removing a substance (see col. 1, lines 55-57 of Henley '410). Among the substances to be delivered, antibacterials and hydroquinone are listed (col. 2, line 11 and col. 4, lines 65-66 of Henley '410). According to Henley '410, the medicament is electrokinetically transported into the treatment site (col. 4, lines 39-41 of Henley '410).

In contrast, as noted above, the present invention discloses a method for treating a skin condition comprising pretreating skin to generate hydrophilic micro-channels by the use of the apparatus disclosed and claimed herein and then topically applying to the pretreated skin without the application of electrical energy a cosmetic composition comprising a water-soluble, poorly water-soluble or insoluble cosmetic agent to the area in which the micro-

channels are present (see paragraphs [0030] to [0033] of the published application). As indicated above, the cosmetic agent according to the present invention is simply placed over the area where micro-channels are present soon after removal of the apparatus such that no electrical energy is applied and the cosmetic agent is delivered by diffusion only (see paragraph [0026] and the examples of the published application). Thus, even if one combines Sintov, Zhang and Henley '410, he or she would obtain a method for delivery of L-ascorbic acid and hydroquinone comprising generating micro-channels and electrokinetically delivering those compounds to the subject's blood. This is not the method recited in claim 14. As claims 18, 20 and 21 depend directly or indirectly from claim 14 and include further recitations thereto, claims 18, 20 and 21 are patentable over Sintov in view of Zhang and Henley '410 and the rejection of these claims under 35 U.S.C. 103(a) should be withdrawn.

Claims 14-17, 19, and 22-24 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over "Enabling topical immunization via microporation: a novel method for pain-free and needle-free delivery of adenovirus-based vaccines" to Bramson (referred herein as "Bramson") in view of U.S. Patent Application No. 2002/0161324 to Henley (referred herein as "Henley '324") in view of Zhang. The Office Action indicates that Bramson teaches a system and method for intradermal delivery of an agent comprising generating a plurality of micro-channels in the skin. The Office Action further indicates that Bramson teaches applying a vaccine via the use of a patch applied to the skin after the channels are created, however, Bramson fails to teach a cosmetic composition comprising a cosmetic agent and a carrier devoid of permeation enhancers. The Office Action states that Henley '324 teaches an electrokinetic delivery device. Zhang teaches producing transient pores in the skin to facilitate the transdermal delivery of a cosmetic agent composition comprising a cosmetic agent, an acceptable carrier that is devoid of permeation enhancers. The Office Action states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the device and method of Bramson to apply the patch containing the cosmetic agent and carrier as taught by Zhang to the skin after micro-channel formation in order to provide a means to improve the appearance of the skin.

What Bramson actually discloses is a method of immunization whereby a vaporization process is used to remove tiny areas of the stratum corneum creating microscopic pores that

enabled topical immunization using an adenovirus vaccine as a vector for genetic vaccination (see abstract and p. 252, left column of Bramson). Bramson does not disclose a method for treating a skin condition in a subject comprising generating micro-channels in an area of the skin of a subject by the apparatus of the present invention and topically applying a cosmetic composition comprising a water-soluble, poorly water-soluble or water-insoluble cosmetic agent to the area of the skin where micro-channels are present.

Henley '324 does not remedy the deficiencies of Bramson. Like the other Henley reference, Henley '324 discloses a method of treatment by electrokinetic self-administration of a medicament into a treatment site of an individual (see paragraph [0017] of Henley '324). According to Henley '324, a hand-held device electrokinetically drives the medicament into the treatment site (see paragraph [0017] of Henley '324). Henley '324 does not disclose a method for treating a skin condition whereby a cosmetic composition comprising a water-soluble, poorly water-soluble or water-insoluble cosmetic agent is topically applied to an area of the skin where micro-channels are present and the delivery of the cosmetic agent is by diffusion only and without the application of electrical energy.

Zhang does not remedy the deficiencies of Bramson and Henley '324. Zhang discloses applying an electric pulse to a region of the skin substantially contemporaneously with a composition comprising L-ascorbic acid (see col. 3, lines 61-64 of Zhang). Thus, even if one combines Bramson, Henley '324 and Zhang, he would obtain a method for generating micropores and electrokinetically delivering a composition comprising L-ascorbic acid. He would not obtain a method for treating a skin condition comprising generating hydrophilic micro-channels by the apparatus disclosed in the present invention and topically applying a cosmetic composition comprising a water-soluble, poorly water-soluble or insoluble cosmetic agent to the area in which the micro-channels are present (see paragraphs [0030] to [0032] of the published application). Thus, claims 14-19, and 22-24 are patentable over Bramson in view of Henley '324 and Zhang, and the rejection of these claims under 35 U.S.C. 103(a) should be withdrawn.

Claims 18, 20, and 21 have been rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Bramson in view of Henley '324 in view of Zhang as applied to claims 14 and 15, and further in view of Henley '410. In reference to claim 18, the Examiner indicates

that Bramson in view of Henley '324 and Zhang teaches the device and method of claim 15 but fails to teach wherein the cosmetic agent is hydroquinone. The Examiner further indicates that Henley '410 teaches delivery of cosmetic agents to the skin that can include hydroquinone. The Examiner states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the device and method of Bramson in view of Henley '324 and Zhang to deliver hydroquinone in order to remove pigmentation from hyperpigmented areas of the skin.

In reference to claims 20 and 21, the Office Action indicates that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the device and method of Bramson in view of Henley '324 and Zhang to include an antibacterial agent in the composition as taught by Henley '410 in order to inhibit bacterial growth.

Applicants respectfully disagree with these statements. As detailed above, Bramson teaches a method for immunization comprising generating microscopic pores that enabled topical immunization using an adenovirus vaccine as a vector for genetic vaccination. Henley '324 discloses a method of treatment by electrokinetic self-administration of a medicament into a treatment site of an individual. Zhang discloses applying an electric pulse to a region of the skin substantially contemporaneously with a composition comprising L-ascorbic acid. Henley '410 discloses a portable, self-contained, hand-held electrokinetic device for delivering or removing a substance including hydroquinone or an antibacterial agent. If one combines Bramson, Zhang, Henley '324 and Henley '410, one would obtain a method for generating micropores in the skin and applying hydroquinone or an antibacterial agent, whereby hydroquinone or the antibacterial agent are delivered electrokinetically.

In contrast, the present invention discloses a method for treating a skin condition comprising generating micro-channels by the apparatus of the invention, and topically applying a cosmetic composition comprising a water-soluble, poorly water-soluble or water-insoluble cosmetic agent to the area where micro-channels are present. As indicated above, the delivery of the cosmetic agent is by diffusion only, not electrokinetically. Thus, claim 14 is patentable over the combination of Bramson, Zhang, Henley '324 and Henley '410. As claims 18, 20 and

21 depend directly or indirectly from claim 14, these claims are patentable as well, and the rejection of these claims under 35 U.S.C 103(a) should be withdrawn.

In view of the above, it is respectfully submitted that all current rejections have been overcome and should be withdrawn. Accordingly, the entire application is believed to be in condition for allowance, early notice of which would be appreciated. Should the Examiner not agree, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of this application.

Respectfully submitted,

A handwritten signature in cursive script, reading "Allan A. Fanucci".

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